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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/682,130	10/07/2003	Dennis M. Klinman	4239-66902-01	1348

36218 7590 06/22/2007
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EXAMINER	
ARCHIE, NINA	
ART UNIT	**PAPER NUMBER**
1645	
MAIL DATE	**DELIVERY MODE**
06/22/2007	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	**Application No.** 10/682,130	**Applicant(s)** KLINMAN ET AL.	
	Examiner Nina A. Archie	**Art Unit** 1645	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on 30 October 2006.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) 1-7,10-30 and 33-47 is/are pending in the application.

4a) Of the above claim(s) 42 is/are withdrawn from consideration.

5)☒ Claim(s) 43-47 is/are allowed.

6)☐ Claim(s) 1-7,10-30 and 33-41 is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date 10/7/2003, 4/4/2005, 2/20/2007.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

1. This Office Action is responsive to Applicant's amendment and response filed on 3-16-07. Claims 1-7, 10-30, and 33-47 are pending. Claims 8-9 and 31-32 are cancelled. Claims 1, 20 and 23 are amended. Claim 42 is withdrawn from consideration. Claims 43-47 are new.

Information Disclosure Statement

2. The information disclosure statement filed April 4, 2005 was signed on 10/26/2006 and considered in the Office Action on 11/15/2006. The information disclosure statement filed on 10/7/2003 and 2/20/2007 has been considered. Initialed copies are enclosed.

Rejections Withdrawn

3. In view of the Applicant's amendment and remark following rejections are withdrawn.

a) Rejection to claims 20-22 under 35 U.S.C. 112, second paragraph, page 16 paragraph 2 is withdrawn in light of applicant's amendment thereto.

Claim Rejections Maintained

35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

4. Claims 1-41 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a method of treating inflammatory lung disease,

comprising administering a therapeutically effective amount of a suppressive oligodeoxynucleotide SEQ ID NO. 1 to a subject having or at risk of developing inflammatory lung disease in vivo, does not reasonably provide enablement for an *in vitro* method of treating inflammatory lung disease, comprising administering a therapeutically effective amount of suppressive oligodeoxynucleotide comprising SEQ ID NOs. 2-25. Furthermore, the specification does not reasonably enable an *in vivo* method of inhibiting inflammatory lung disease in a subject, animal or human, comprising administering a therapeutically effective amount of a suppressive oligodeoxynucleotides to a subject having or at risk of developing inflammatory lung disease. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with the claimed invention.

Applicant arguments:

That the one of skill in the art could readily make and use the claimed ODNs without undue experimentation and submit a Wands analysis:

(A) Breadth of the claims: The claims are limited to the treatment of an inflammatory lung disease using a suppressive ODN that is at least about 8 nucleotides in length, forms a G-tetrad, has a CD value of greater than about 2.9, and comprises at least two guanosines, wherein the oligodeoxynucleotide is from about 10 to about 30 nucleotides in length. Claims 17 and 41 recite specific nucleic acid sequences of use in the claimed methods.

(B) The nature of the invention: The claims are directed to methods of treatment that utilize nucleic acid sequences.

(C) The state of the prior art: The synthesis of ODNs is well known in the art, as is the administration of ODNs to a subject of interest. There are art-recognized models for testing therapies for the treatment of inflammatory lung disease.

(D) The level of ordinary skill in the art: The level of skill of a molecular biologist and/or pulmonologist is high.

(E) The level of predictability in the art: The production of ODNs with specified characteristics is routine. There are art recognized models for inflammatory lung disease (such as the one described in the examples section) that can be used to confirm the effect of an ODN of interest. The administration of agents to a subject for the treatment of inflammatory lung disease is described (see the specification, page 24, line 9 to page 30, line 10); the pharmaceutical formulations and methods of administration are routine to one of skill in the art.

(F) The amount of direction provided in the specification: The specification discloses the physical characteristics of ODNs of use, namely that they (1) are 10-30 nucleotides in length, (2) have a CD value of greater than about 2.9 (for example, see the specification on page 20, lines 15-24), and (3) form a G-tetrad (for example, see the specification on page 20, lines 7-14). General classes of ODNs that have these characteristics are provided (see the specification on page 21, lines 1-10), and at least 25 examples of suppressive ODNs are provided (see the specification on page 21, lines 11-21, and SEQ ID NOs: 1-25). In addition, pharmaceutical compositions and methods of administration of ODNs are described in the specification (see page 24, line 9 to page 30, line 10). Methods for confirming the effectiveness of an ODN, such as by monitoring lung function are disclosed (see the specification at page 30, line 11 to page 31, line 15).

(G) The existence of working examples: Numerous exemplary ODNs of use are described in the specification (see, for example, page 21, lines 15-21 and SEQ ID NOs: 1-25). The effectiveness of these ODNs in inhibiting an immune response in vitro is disclosed (see Example 2). The use of an exemplary ODN (SEQ ID NO: 1) in an animal model of inflammation is described in the specification (see Example 3). Thus, a working example is provided.

(H) The quantity of experimentation required: There is substantial guidance provided on the synthesis of ODNs and formulation of ODNs for delivery to a subject (see, for example, page 19, line 26 to page 24, line 7). The synthesis of ODNs is automated and routine. Thus, only limited experimentation is required to practice the claimed invention.

Examiner's Response to Applicant's Arguments:

A) The Examiner accepts that that the claims have been amended to provide that the oligodeoxynucleotide is from about 10 to about 30 nucleotides in length. The examiner accepts that the claims are limited to the treatment of an inflammatory lung disease using a suppressive ODN that is at least about 8 nucleotides in length, forms a G-tetrad, has a CD value of greater than about 2.9, and comprises at least two guanosines, wherein the oligodeoxynucleotide is from about 10 to about 30 nucleotides in length. The Examiner accepts that claims 17 and 41 recite specific nucleic acid sequences for use in the claimed method. However the lower length of 10 nucleotides is not shown in any in Table 1, which is a list of the suppressive ODNs. Therefore the Examiner disagrees with the Applicant's assertion that one of skill in the art could readily make and use the claimed ODNs without unde experimentation.

B) The Examiner accepts that the claims are directed to methods of treatment that utilize nucleic acid sequences. However the claimed method is not only directed to methods of treatment but also to methods of inhibiting that utilize nucleic acid sequences. As discussed previously, the state of the art indicates that the state of the art for treating and preventing inflammatory lung disease are using current treatments such as anti-inflammatory medications. Although inflammatory lung disease can be treated there is no treatment for recurrence or prevention of the full development of the disease. The standard therapy for treating inflammatory lung disease is corticosteroids. However they also have limitations in their treatment and cannot inhibit inflammatory lung disease (see Broide et al 1998 Immunostimulatory DNA Sequences Inhibit IL-5, Eosinophilic Inflammation, and Airway Hyperresponsiveness in Mice The Journal of Immunology p. 7054 and Bernard GR 2005 Acute respiratory distress syndrome: a historical perspective. *American Journal Respiratory Critical Care Med.* 2005 Oct 1;172(7):798-806). Therefore the Examiner disagrees with the Applicant's assertion that one of skill in the art could readily make and use the claimed ODNs without under experimentation.

C) The examiner accepts that the synthesis of ODNs is well known in the art, as is the administration of ODNs to a subject of interest and that there are art-recognized models for testing therapies for the treatment of inflammatory lung disease.

(D) The examiner accepts that the level of ordinary skill in the art is of a molecular biologist and/or pulmonologist is high.

(E) The examiner accepts that there are art recognized models for inflammatory lung disease (such as the one described in the examples section) that can be used to confirm the effect of an ODN of interest and the administration of agents to a subject for the treatment of inflammatory lung disease is described (see the specification, page 24, line 9 to page 30, line 10). The examiner accepts the pharmaceutical formulations and methods of administration are routine to one of skill in the art. However the examiner disagrees that the level of predictability in the art and the production of ODNs with specified characteristics is routine. The specification teaches a method of treating inflammatory lung disease with suppressive oligodeoxynucleotides in a subject however the specification does not teach a method of inhibiting/preventing inflammatory lung disease nor does the state of the art teach any method of inhibiting/preventing inflammatory lung disease administering a suppressive oligonucleotide.

(F) The examiner accepts the amount of direction provided in the specification: The specification discloses the physical characteristics of ODNs of use, namely that they (1) are 10-30 nucleotides in length, (2) have a CD value of greater than about 2.9 (for example, see the specification on page 20, lines 15-24), and (3) form a G-tetrad (for example, see the specification on page 20, lines 7-14). General classes of ODNs that have these characteristics are provided (see the specification on page 21, lines 1-10), and at least 25 examples of suppressive ODNs are provided (see the specification on page 21, lines 11-21, and SEQ ID NOs: 1-25). In addition, pharmaceutical compositions and methods of administration of ODNs are described in the specification (see page 24, line 9 to page 30, line 10). Methods for confirming the effectiveness of an ODN, such as by monitoring lung function are disclosed (see the specification at page 30, line 11 to page 31, line 15). However the examiner disagrees that the ODNs administered in the method can inhibiting/preventing inflammatory lung disease because there no examples show in the specification of inhibiting/preventing inflammatory lung disease. Also the specification does not show any nucleotides at the lower range of 10-30 nucleotides in length.

(G) The examiner accepts working examples of the ODNs of use described in the specification (see, for example, page 21, lines 15-21 and SEQ ID NOs: 1-25). The examiner accepts the effectiveness of these ODNs in inhibiting an immune response in vitro as disclosed in Example 2. The examiner accepts the use of ODN (SEQ ID NO: 1) in an animal model of inflammation is described in the specification as disclosed in Example 3. However there is no working example for inhibiting/preventing inflammatory lung disease in vivo and there is no working example for treating inflammatory lung disease in vitro. Therefore there is no correlation between an in vivo and vitro example of a method of inhibiting/preventing inflammatory lung disease. There is also no correlation between in vivo and vitro example of a method of treating inflammatory lung disease. Therefore the Examiner disagrees with the Applicant's assertion that one of skill in the art could readily make and use the claimed ODNs without under experimentation.

(H) The examiner accepts that there is substantial guidance provided on the synthesis of ODNs and formulation of ODNs for delivery to a subject (see, for example, page 19, line 26 to page 24, line 7). The examiner accepts that the synthesis of ODNs is automated and routine. However there is only guidance to the method of inhibiting/preventing inflammatory lung disease in vitro. There is only guidance to the method of treating inflammatory lung disease in vivo. Therefore the Examiner disagrees with the Applicant's assertion that one of skill in the art could readily make and use the claimed ODNs without under experimentation.

5. Claims 1-41 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter, which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. In the instant case, the claim is drawn to a method of treating or inhibiting inflammatory lung disease in a subject, comprising administering a therapeutically effective amount of a suppressive oligodeoxynucleotide to a subject having or at risk of developing inflammatory lung disease, wherein the suppressive oligodeoxynucleotide is at least about 8 nucleotides in length, forms a G-tetrad, has a CD value of greater than 2.9, and comprises at least two guanosines, thereby treating or inhibiting the inflammatory lung disease. The recitation of "at least about least 8 nucleotides in length", "forms a G-tetrad", and "at least two guanosines" does not convey a common structure. Further the claim recites open claim language and the exact structure of the vast genus of suppressive oligodeoxynucleotide cannot be envisioned. The oligonucleotides recited in the pending claimed genus would not clearly apprise one skilled in the art that the inventors had possession of the claimed genus and all species encompassed thereby as of the filing date. The structure of these oligonucleotides has not been specifically defined. The claims do not set forth the specific structure of the claimed oligonucleotides and it is not clear if the claims or specification give the structure and a function of the oligonucleotide, as required by written description guidelines.

Applicant arguments:

With regard to written description: The specification discloses the physical characteristics of ODNs of use, namely that they (1) are 10-30 nucleotides in length, (2) have a CD value of greater than about 2.9 (for example, see the specification on page 20, lines 5-24), and (3) form a G-tetrad (for example, see the specification on page 20, lines 7-14). General classes of ODNs that have these characteristics are provided (see the specification on page 21, lines 1-10), and at least 25 examples of suppressive ODNs are provided (see the specification on page 21, lines 11-21, and SEQ ID NOs: 1-25). In addition, pharmaceutical compositions and methods of administration of ODNs are described in the specification (see page 24, line 9 to page 30, line 10). Methods for confirming the effectiveness of an ODN, such as by monitoring lung function are disclosed (see the specification at page 30, line 11 to page 31, line 15).

The Office action (see page 14) cites the Guidelines for Examination of Patent Applications under 35 U.S.C. § 112, paragraph 1 as stating "possession may be shown in a variety of ways including description of an actual reduction to practice, or by showing the invention was 'ready for patenting' such as by disclosure of drawings or structural chemical formulas that show the invention was complete, by describing distinguishing identifying characteristics sufficient to show that the applicant was in possession of the claimed invention." Applicants would like to draw the Examiner's attention to a drawing (Figure 1A), which illustrates the specific structure of an oligodeoxynucleotide that forms a G tetrad. As described in the specification, a G tetrad involves the planar association of guanosines in a cyclic Hoogsteen hydrogen bond arrangement. The specification provides information on specific physical and stereochemical properties of these structures (see, for example, page 20). G-tetrads can be classified based on the circular dichromotism (CD) values. Specific lengths of ODNs of use are provided. In addition, a specific subclass of ODNs of use is described: ODNs with TTAGGG repeats. Moreover, 25 specific examples of ODNs of use are provided as SEQ ID NOs: 1-25 (see page 21).

An applicant seeking to claim a genus of compounds, such as a nucleic acid must provide a "representative" number of species within the genus. It is well established that an Applicant need not disclose every species encompassed by a claim (In re Angstadt, 537 F.2d 498, 190 USPQ 214 (CCPA 1976). In the present application, ODNs with specific physical and stereochemical properties are disclosed. The structure of these molecules is clearly set forth. In addition, 25 examples are provided. Thus, there clearly is sufficient written description for the claimed ODNs.

Examiner's Response to Applicant's Arguments:

Examiner accepts that the specification discloses the physical characteristics of ODNs of use, namely that they (1) are 10-30 nucleotides in length, (2) have a CD value of greater than about 2.9 (for example, see the specification on page 20, lines 5-24), and (3) form a G-tetrad (for example, see the specification on page 20, lines 7-14). General classes of ODNs that have these characteristics are provided (see the specification on page 21, lines 1-10), and at least 25 examples of suppressive ODNs are provided (see the specification on page 21, lines 11-21, and SEQ ID NOs: 1-25). In addition, pharmaceutical compositions and methods of administration of ODNs are described in the specification (see page 24, line 9 to page 30, line 10). Examiner accepts the method of utilizing the ODNs. However examiner disagrees with the range of 10-30 nucleotides in length. Table 1 discloses the length of the nucleotides, whereby none of the ODNs have the lower range of 10 nucleotides in length.

Conclusion

Status of the Claims

6. Claims 43-47 are allowed.
Claims 1-7, 10-30, and 33-41 are rejected.
Claim 42 is withdrawn.

THIS ACTION IS MADE FINAL. Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Nina A. Archie whose telephone number is 571-272-9938. The examiner can normally be reached on Monday-Friday 8:30-5:00p.m..

If attempts to reach the examiner by telephone are unsuccessful, the examiner supervisor, Jeffrey Siew can be reached on 571-272-0787. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

Nina A Archie
Examiner
GAU 1645
REM 3B31

MARK NAVARRO
PRIMARY EXAMINER